National Guidelines for Collection, Usage, Storage, and Export of Human Biological Materials 2020

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FORWARD

The use of Human biological Material (HBM) for clinical and research purposes are indispensible and contributes to knowledge and welfare of Human beings but many ethical issues are related to the use of HBMs which require regulations to ensure the protection of individuals' self-determination, integrity and privacy.

Pakistan Health Research Council (PHRC), Ministry of National health Services, Regulation and Coordination, Islamabad, is the secretariat of National Bioethics Committee (NBC), Pakistan. NBC developed this document "National Ethical Guidelines for collection, usage, storage and export of Human Biological Material and published in 2016. All right of this document are reserved with NBC and NIH.

National Institute of Health (NIH) is a focal point for Biosafety and Bio security as one of the core abiding of International Health Regulation (IHR) and Global Health Security Agenda (GHSA). The revised version Ethical Guidelines for usage, storage and export of Human Biological Material (2019) includes a section in seeking approval from NIH as National Focal Point for Biosafety/Biosecurity.

The Strategic Export Control Division (SECDIV) is a part of the Ministry of Foreign Affairs (SRO 499(I)/2009), to administer export controls.

SECDIV is the licensing Authority for items mentioned in the Control Lists (SRO) and those non-listed items. It also coordinates enforcement of the Act. Export Control (Licensing and Enforcement) Rules (SRO 450(I)/2009) set out procedures for licensing and implementation of Export Control Act. The revised version of the guidelines includes the sections about seeking Export License from SECDIV, Ministry of Foreign Affairs (MoFA).

The Current Guidelines are developed to provide investigators, researchers and IRBs/ERC/REC/ERBs with clear guidance regarding the use of human biological materials in research, particularly with regard to informed consent and Material Transfer Agreement for research in this area.

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National Institute of Health

PREFACE

Collection, use transportation of Human Biological Materials (HBM) especially for research purposes has greatly increased all across the globe. Exchange of HBM between institutions is essential in the pursuit of the advancement of science. The importance of the growth of this field cannot be denied but concurrently this also raises many ethical, safety and security issues that must be addressed.

The nature of the study of biology and its various offshoots such as genomics, proteomics or metabolomics (also now known as omics) has made such collaborations unavoidable. Recent advances in the field of genetics, biotechnology and bioinformatics have made it possible for researchers to access not only the health related information but also other personal information including the identifiable information with the use of HBM. This potentially exposes individuals and in many cases communities to psychological harms, including stigmatization and possibilities of exploitation. In Pakistan, as is generally in any developing country, it is important to understand the emerging ethical challenges related to the use of HBM, so as to avoid such issues which can undermine trust of the community for research and researchers. A proper framework / guidance needs to be established to make these activities ethically sound, prevent their misuse and ensure authorized/peaceful uses.

PRIMARY OBJECTIVES

Pakistan Health Research Council (PHRC), National Institute of Health (NIH) and Ministry of Foreign Affairs (MoFA) has developed this document to facilitate researchers and, IRB/ERC/REC/ERB members while conducting or reviewing research on any kind of HBM in an ethical manner. This document discusses multiple aspects of HBM usage in medical research and provides ethical guidelines regarding collection, usage, storage and export of HBM to prevent their misuse. These guidelines address important ethical issues that need to be considered when conducting research on HBM that:

1. Have already been collected, or will be collected, from patients for routine investigation/treatment;
2. Involves collection of HBM solely for the purpose of bio-banking and subsequent research.
3. These guidelines may also be used by regulatory authorities for drafting legislations regarding the collection, usage, storage and export of HBM.
4. It is recognized that with the rapid pace of advancement in biomedical science these guidelines will require regular review and revision. NBC will welcome input and comments to keep these guidelines relevant and robust.

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1. Introduction

Human biological material (HBM) means any materials of human origin. These include, but are not limited to, blood, urine, saliva, pus or other bodily fluids; tissues; hair or nails; placenta, umbilical cord & cord blood; sperms, oocytes, left over frozen embryos following IVF & other products of conception; excess pathology tissues, and waste surgical tissues.[1]

1.1 Purposes for collection of HBM

Emerging technologies and advances in biology have led to the discovery of multiple or varied uses of HBM, **simultaneously raising the potential of their misuse.** Common utilities of HBM are enumerated below:

1.1.1. Clinical purpose

HBM is widely used for clinical purposes to facilitate diagnosis and prognosis of diseases, and also collected through therapeutic surgical interventions (excision of tissue, a segment of organ or even the whole organ) or for donation/transplant purpose.

1.1.2. Research purpose

Medical research, be it clinical, basic or genetic, aims to improve life. All these types of research involve human participants. The collection of HBM may be done for research diagnosis, prognosis and treatment of the disease, whereas basic research attempts to understand cellular, molecular, and pharmaco-genetic aspects of disease.[2]

1.1.3. Commercial purpose

Advances in the field of biotechnology have resulted in the commercial availability of numerous therapeutic and other

products which are developed from HBM, for example the use of human hair and placenta in cosmetic industry. HBM also carries great significance in pharmaceutical industry where it can be used as raw material or as a precursor for research activities. These utilities have made the commercial use of HBM plausible. The most prominent example is the HeLA cells from Henrietta Lacks the first 'immortal' cells to grow in vitro. These have been sold all around the globe since 1950s.[3]

1.1.4. Biobanking or Archiving of human biological material

Though HBM is most commonly collected to gain immediate clinical information, but modern research directions in medical science such as omics and personalized medicine have introduced the concept of biobanking.

By definition, a biobank is a long-term storage & conservation facility for biological specimens, to support future scientific investigation. These can be commercial (for-profit companies are involved in procurement, handling, and distribution of human biological materials); public (owned by the Government); or public-private partnership. Disease- oriented biobanks usually have a hospital affiliation through which they collect samples representing a variety of diseases to look for biomarkers affiliated with disease.5 Population-based biobanks take samples from large numbers of all kinds of people to identify biomarkers for disease susceptibility in a general population. Biobanks can serve an important purpose for investigating the basis of disease, particularly when combined with health registries and population surveys.

1.1.5. Education purpose

HBM is also widely used in teaching and education. Medical students study and analyze blood urine and other body fluids. Studies of histopathology require the examination of various tissue samples including surgically resected tumors or diseased organs to

distinguish between normal and diseased cells. Donated cadavers are used to teach anatomy to students about all the regions of the body. Preservation of surgically resected tumors or diseased organs (taken at autopsy) in medical museums (to illustrate disease) is also a common practice in some medical schools.

1.2. Categories of HBM

HBM are classified into different categories based on the purpose of collection and potential of human biological material to identify an individual, alone or in combination with other information. The categories are as follows:

1.2.1. Repository collections

Specimens collected for clinical purposes are stored by diagnostic laboratories ranging from few days to as long as several years after use. These stored samples constitute repository collections which can include;

I. **Identified Specimens:** The materials are labeled with a direct identifier (e.g., name, personal health number). Materials and any associated information are directly traceable back to a specific individual

II. **Unidentified Specimens:** For these specimens, identifiable personal information was not collected or, if collected, was not maintained and cannot be retrieved by the repository.

1.2.2. Research Samples:

Samples collected for research use include

I. **Coded HBM:** Materials which do not contain direct identifiers rather codes are used for identification of specimens to maintain the confidentiality. Key that links the codes to individual is retained usually by principal investigator and depending on

access to that code it may be possible to re-identify specific individuals.

II. **Anonymized HBM:** Materials are irrevocably stripped of direct identifiers, a code is not kept to allow future re-linkage, and risk of re-identification of individuals from remaining indirect identifiers is low or very low.

III. **Anonymous HBM:** Materials never had identifiers attached to them and risk of identification of individuals is very low.

1.3. Export or import of HBM

Transport of HBM from one country to another could be for a number of reasons. Potential reasons for export of HBM are discussed below;

1.3.1. Clinical utility:

Medical science is advancing at a very fast pace which has resulted in a gap between the developed and developing countries regarding the diagnostic and treatment facilities for various ailments. One of the main reasons for sending HBM overseas from developing countries is lack of availability of the required diagnostic or analytical facilities in the home country to facilitate diagnosis of a health problem.

1.3.2. Research purposes:

Multinational collaborations in the field of health or biomedical research are now common and require sharing of resources, manpower, samples and technologies between countries to understand the health issues in different parts of the world. Although such collaborations are not uncommon between developed countries. HBM is being exported from developing countries to technologically advanced countries for research purposes due to limited scientific infrastructure available in the developing world.

1.3.3. Biobanking:

The emerging interest towards personalized medicine requires access to data, and bio-bank materials are the obvious source of such data. These biobanks may be commercial, public or public-private partnership. For decades HBMs from developing countries particularly African countries along with the respective data are being sent to and stored in developed countries (where bio-banking facilities are available) for uncertain secondary use.[8] It is common knowledge in developing countries that HBM exported without Material transfer Agreement MTA (for clinical or research purposes) may be (or may have been) re-exported and bio-banked.

2. Ethical issues in research involving the use of HBM

2.1. Informed Consent

With the advancement in biomedical research the ethical and legal issues in research on human biological samples are also increasing. In Pakistan currently no ethical guidelines or legal precedent is available for this issue. Most of contemporary ethical issues are related to absent, uninformed, or poorly informed and understood consent from individuals for the use of their human biological samples. At times even outright deception can be employed. The recent case of Diabetes Project with Havasupai Indian tribe in the USA is one such example of research deception and misconduct.[9] Obtaining a proper informed consent, comprehended and given voluntarily by the individual from whom HBM is sought (even if anonymized), lies at the heart of ethical research. The absence of such consent means disrespecting and violating the rights of individuals to control the use of their bodily tissues for research even if it is considered of potentially little or no risk to them. An appropriate informed consent is also a means to protect individuals and communities from potential harms

including inadvertent breach of confidentiality, stigmatization, and emotional and psychological repercussions.

In industrialized countries, the field of medicine is evolving towards personalized or precision medicine that relies on patients' genetic information. This has lead biomedical research towards individual genome sequencing raising ethical issues about appropriate and robust informed consent. A recent initiative by the US government called Precision Medicine Initiative (PMI) aims to revise the 25 year old Common Rule known as codified at 45 CFR part 46.[10] If approved, proposed amendments will make it easier for researchers to perform research using bio-banked materials without renewed consent if the donor had previously consented for storing his or her samples in a bio-bank. While this may facilitate research, the proposal has given rise to several potentially troubling ethical issues that are being currently discussed.

Research, whether national or multinational in nature, using HBM from people from countries like Pakistan adds complexities to the informed consent process due to local contexts. These include collective, hierarchical, and family centered decision making processes rather than by individuals.[11] In addition, the tremendous existing power differentials (due to levels of education, social status, economics, etc.) between physicians/researchers and research participants makes the research participant especially vulnerable to exploitation and deception. It is important that physicians/researchers be aware of and are sensitive to these factors and they must employ appropriate steps to facilitate and ensure that the informed consent process is not coercive but respects the rights of research participants to make choices regarding use of their tissues.

The reasons and consequences for obtaining the consent must be explicitly explained to the donor/owner/ parents/legal guardians etc. when biological material is to be

obtained from children, incapacitated adults, and other vulnerable groups such as prisoners, the proposed research should directly relate to them or their disease, and their inclusion should be based on scientific reasons and not on the convenience of the researcher. In the case of minors/incapacitated adults the consent should be taken from parents/legal guardians. For mature minors who require a legal consent from guardians, researchers should ensure that they understand the proposed research on their tissues and also seek their permission/assent for it.

2.2. Ownership of HBM

Once a tissue or organ is collected or excised out of the body (for any reason) the question of ownership of that HBM arises. This is a complex issue as humans do not have legal or propriety rights on their organs and tissues. However, some believe that in the medical and scientific realm it may be considered as property.[12]

Several concepts have emerged as a result of this debate on ownership of HBM. The person from whom the HBM originated is referred to as the owner (or contributor a term being used more often), who is the person who ought to set the terms and conditions for the use of that HBM through the process of informed consent. The institution that takes the HBM then becomes the custodian of the tissues and agrees to use this HBM as outlined by the consent. If the custodian has to send this HBM to another party (if allowed by the consent) then it is custodian's responsibility to make sure by having a Material Transfer Agreement (MTA) that use of this tissue by the next party which becomes the possessor who, still remains confined to the terms of the consent under which it was taken.

2.3. Privacy and Confidentiality

An individual's health related information is considered sensitive and must be treated as private and confidential.

The custodian of HBM should be clear about the intended use of that material and related information. This information must be disclosed and permission sought from the owner in the form of Informed consent as mentioned earlier. HBM must not be used beyond owner's will. If custodian needs to send HBM to a third party then he/she must ensure that privacy and confidentiality terms as set between owner and custodian are not compromised and that third party consents to abide by those terms. It is also advisable that prior to the material transfer to third party, any identifiable information be coded to further protect the confidentiality.

2.4. Commercial uses and Benefit sharing

The Universal Declaration on Bioethics and Human Rights states in Article 15, "Benefits resulting from any scientific research and its applications should be shared with society as a whole and within the international community, in particular with developing countries"[13]. The commercial use of HBM without sharing benefits with the donor is unfair as it violates principle of reciprocity. However a fine balance needs to be maintained as benefits may raise ethical concerns regarding inducement. Access to medical care and/or drugs stemming from the research, provision for new diagnostics, support for health services and capacity-building facilities for research purposes may be regarded as suitable forms of compensation or benefit sharing.

3. Guidelines for collection, usage and storage of Human Biological Materials

Human biological material HBM may be taken for many purposes as enlisted in this document. Collection, storage and use of HBM for research and other purposes exclusively require a valid informed consent. If HBM is taken for clinical purpose and further research on these samples is planned then consent for the diagnostic and treatment purposes must be separate from the consent for the use

of remaining samples in research.[14] A clear explanation should be given to the potential research participants. In cases where stored biological samples are to be used when no consent was obtained for research, or the samples are not individually identifiable, and there is no potential harm to persons from whom the samples were obtained, it is still required that Research Ethics Committee's approval be sought prior to initiating research. Different approaches have been suggested to obtain informed consent for HBM[9] (Annex II) -

3.1 Right to Know

At the time of collection of HBM individuals have the right to know for what purpose this material will be used, the nature of research risk, where will it be stored, and for how long is it going to be stored.

3.1.1. Consent form must be explicit and separate from that used for routine surgery/procedure; it must clearly mention the use of HBM in research.

3.1.1. Blanket/generic consent for future research in which purpose of the research and other important information is unknown is not recommended (Annex I) -.

3.1.1. Ideal consent in which patients have the most control is a tiered consent. In this consent different levels of permissions are granted to researcher in an explicit way. Modified WHO tiered consent form is available as (Annex II) -.

3.1.1. Tiered consent must contain at least the following important information:

i. Type of HBM collected and the purpose of its collection

ii. Whether HBM will be used further for other research unconnected with this research, including the type of disease in which future research might be done.

iii. Whether HBM will be exported to other country/ies. Mention names of country/ies. Give provision to participant to mention exceptions for any country where participant might not want to send his/her samples. (Guidelines for Export of HBM are mentioned below).

iv. What will be the duration of sample storage and when, where and how will it be disposed or destroyed?

v. Whether this sample will be used for biobanking (either in public or commercial biobank). Options must be given to participant that they may delinked/anonymized or may keep their sample identifiable.

vi. Whether the consent has clearly explained genetic research. Specific consent explaining what genetic research implies must also be taken if HBM is going to be used for genetics research.

vii. The consent should clearly declare if the sample will be used for commercial purposes and if any methodology will be used for benefit sharing.

viii. How will privacy and confidentiality of the participant be maintained

3.1.2. For research on HBM samples which had been previously collected for routine treatment or diagnostic procedure, it is suggested that consent should be taken from these patients. If this is not feasible or practical, then approval from Institutional Research Ethics Committee (REC)

is mandatory before using these samples in research, providing reasons as to why re-consent is not possible.

3.2 Confidentiality and Privacy

Confidentiality and privacy should be maintained throughout the research.

HBM custodian is responsible to protect and standardize the usage, storage, access, export, & disposal of the tissue.

3.2.1. If samples are sent to third party, all parties must abide by privacy and confidentiality terms.

3.2.2. Confidentiality must be ensured by implementing appropriate security measures to prevent unauthorized access and restrict data.

3.2.3. Prior to sending the HBM to third party identifiable information must be coded

The level of anonymization and process should be approved by the Institutional Research Ethics Committee

3.2.5. Privacy should also be maintained at the time of reporting the results. In case of genetic research it must be ensured that any group or community will not be stigmatized by the research outcome.

4. Guidelines for oversight of Human Biological Material for export

Entities involved in collection, usage, export and storage of HBMs are urged to institute ICP so that risk of misuse or diversion are minimized. ICP guidelines notified by Strategic Export Control Division (SECDIV), Ministry of Foreign Affairs vide Gazette of Pakistan No. 2(24)/2013-SECDIV (P) dated 3 October 2014 may be consulted in this regard

It is strongly recommended that all relevant entities should establish appropriate measures so that all research proposals involving export of HBM are submitted to the NBC/REC for review. It may be noted that procedure for export of human plant and animal pathogens, toxins, genetically modified organisms and any living material whether natural, enhanced or modified either in the form of "isolated live cultures" or as material including living material which has been deliberately inoculated or contaminated with such cultures as mentioned in the control lists is regulated under SECDIV Export Control (Licensing & Enforcement) Rules – 2009.

Many compelling reasons already listed above exist for export of HBM from developing to developed country countries. In addition to research benefits, the exportation of HBM may also have tangible public health benefits because of knowledge transfer.

However, despite potential benefits, export of HBM may result in several ethical and legal implications since it involves collection, storage and distribution of information that may result in harm to individuals or groups. Lack of ethical guidance and regulations regarding procurement and distribution of HBM can pose serious international risk to donors as well as recipients of HBM. Hence Governments where institutions (clinical laboratories or R & D organizations) are involved in import or export of HBM must develop some policies or regulations for controlling import and export of

HBM to safeguard and protect their individuals and communities against any harm or exploitation. Development of such regulations must take into consideration the input of clinicians, scientists, health regulators, lawyers, ethicists and representatives from civil society and especially donors.

All the aforementioned guidelines for the collection, storage and use of HBM in research are applicable for the export of any HBM. Additionally, any institution or researcher who wishes to export HBM from Pakistan must also follow the guidelines below.

4.1 Approval from National Bioethics Committee (NBC)

Approval from National Bioethics Committee (NBC) must be sought before exporting any HBM from Pakistan for research purpose.

4.1.1. Duly filled in application form of NBC-REC (Research Ethics Committee) along with a copy of the proposal must be submitted to NBC for approval. The application form I and guidelines for Collection, Usage, Storage and Export of Human Biological Materials are available at website of NBC.

4.1.1. Approval letter of institutional Ethical Review Committees of exporting institution from Pakistan must also be submitted to the NBC with the application form.

4.1.2. Evidence of ethical clearance from the institutional Ethical Review Committee of the institution where HBM is being exported must also be submitted to NBC.

4.1.1. Copy of Material Transfer agreement (MTA) between the two institutions must also be submitted.

4.2. Export License from Strategic Export Control Division, Ministry of Foreign Affairs

An Export license will be required from SECDIV for export , re-export, transit and transshipment of human, plant and animal pathogens, toxins, genetically modified organisms and any living material whether natural, enhanced or modified either in the form of "isolated live cultures" or as material including living material which has been deliberately inoculated or contaminated with such cultures falling under Export Control on Goods, Technologies, Material and Equipment related to Nuclear and Biological Weapons and their Delivery Systems ACT-2004 (Act No. V of 2004) and Control Lists notified there under (Available at website of Ministry of Foreign affairs. Approval from NBC will be mandatory for seeking SECDIV license.

4.3 Approval from National Institute of Health (NIH)

For export of pathogens, specimen/samples of human or animal origin or their derivatives such as cultures, isolates, or DNA/RNA extract etc., the National Bioethics committee shall refer the proposals to NIH for seeking permission on prescribed format (Annex- IV available at the website of NIH). **The practice of sharing** pathogens, specimen/samples of human or animal origin or their derivatives such as cultures, isolates, or DNA/RNA extract etc **shall not be undertaken without approval from National Bioethics Committee along with permission from NIH in addition to already existing rules and regulations notified by SECDIV.**

4.4. The institution exporting HBM

The institution exporting HBM should be transparent about the purpose for which they wish to export HBM.

4.4.1. The institution exporting HBM should present a valid

purpose for which they wish to export HBM. They must be able to demonstrate to NBC that the purpose for which they are exporting for cannot be achieved within the country. For example researchers sending samples for particular tests that are not available within the country and the results of which can contribute significantly to the knowledge regarding a health problem in their own country is a valid scientific reason to send samples abroad.

4.4.2 Institutional and National Bioethics Committee will evaluate if the justification proposed is acceptable for HBM being transported for research.

4.4.3 A self compliance system will assist in fostering ethical behavior and contribute towards effective compliance of relevant national laws, procedures and guidelines on Collection, Usage, Storage and Export of HBM.

4.5. Written Informed Consent

Any HBM to be exported must be accompanied by the written informed consent from donor (or owner) or his/her legally authorized representative.

4.5.1. Any HBM to be exported must accompany a written informed consent from donor or owner i.e. the person whom tissues belong to or his/her legally authorized representative.

4.5.2. All the requirements of informed consent as described earlier in the consent section must be satisfied for a valid informed consent. Additionally for export purposes the signed consent forms from donor/ owner/ Legally Authorized Representatives (LAR) must explicitly mention that he/she agrees that his/her sample be sent abroad (including the country to which it is being exported) for that specific research.

4.5.3. In cases where it is not possible to submit signed consent forms (in case where researcher has anonymized the samples to be exported or in case the owner or contributor is dead or un-locatable) a copy of the information sheet may be acceptable if researcher assures that the consent was in place. However, this is not recommended and is likely to be an exception rather than a rule.

4.5.4. A waiver to consent of participants may also be granted by NBC in some cases when it is not practically possible to obtain the consent. NBC will evaluate the proposal for following points while considering a waiver:

i The proposed research is expected to contribute significantly to the understanding of some local health problem and that the overall benefit to research is real and substantial

ii Potential risk to the privacy or wellbeing of the participants is minimal e.g. use of unidentified archival specimen

iii The nature of any existing consent relating to collection and storage and use of material

iv Whether the research proposal is an extension of, or closely related to a previously approved research project.

v The justification presented for seeking waiver of consent, including the extent to which it is impossible, difficult or intrusive to obtain consent.

4.6. Appropriate guidelines

Appropriate guidelines must be followed for transportation of HBM

For labeling, packaging and handling, World Health Organization (WHO) guidance on regulations for the Transport of Infectious Substances 2017 must be followed.

4.6.1 Appropriate modes of transport, suitable routes and arrangements with people involved must be planned and arranged in advance in accordance with recommended international standards.

4.6.2 Professional courier services must be used whenever possible.

4.7. Material Transfer Agreement

Material Transfer Agreement between institutions of both importing and exporting countries must be signed.

4.7.1 A Material transfer agreement (MTA) must be signed by the institutions of both importing and exporting countries whenever they wish to transport the HBM.

4.7.2 MTAs should define the rights, obligations and restrictions for both the importer and exporter with respect to the materials and any derivatives, and any confidential information exchanged with the material.

4.7.3 It must also encompass intellectual property rights (actual or potential) of the material and any derived products, permitted use of material or information exchanged, liabilities of both parties (including storage, distribution and disposal of HBM), arrangements for confidentiality maintenance of provider information, rights to publication of recipient research results and

any other associated legal issues that the provider and recipient may wish to specify in the transaction.

4.7.4 Material Transfer Agreement must include appropriate clauses for restricting re-transfer including certificate of non-diversion assurance/certificate.

4.7.5 Material Transfer Agreement to be verified by the Health Department of the importing country. This will be attached with export application for items of CLs notified by the GoP under Export Control on Goods, Technologies, Material and Equipment related to Nuclear and Biological Weapons and their Delivery Systems Act-2004.

4.7.6 End-User Undertaking: We (the person or body named) certify that we are the end-user of the goods which are to be supplied by the exporter (named) will be used for peaceful purpose and, will not be deviated from the stated end use. We further certify that neither the goods nor replicas and derivatives will be used for any purpose connected with biological weapons; that they will not be re-exported or otherwise re-sold or re- transferred if it is known or suspected that they are intended or likely to be used for malicious purposes.

It is mandatory to submit a copy of MTA to NBC while seeking permission for the export of HBM. The Guidelines for Drafting an MTA can be found at the WHO website and Sample MTAs can be found on website of Public Health England and National Institute of Health (USA) (The links are provided at the end). (Template MTA agreement is attached as Annex III.

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6. Government Documents available at:

1. http://www.mofa.gov.pk/secdiv/documents/ICP-Guidelines.pdf .
2. http://www.mofa.gov.pk/secdiv/documents/Doc-3,Licensing%20&%20Enforcement%20Rules.pdf)
3. http://www.mofa.gov.pk/secdiv/documents/Doc-1%20Export%20Control%20Act-2004.pdf
4. http://www.mofa.gov.pk/secdiv/documents/Control-Lists-Dec16.pdf).
5. http://nbcpakistan.org.pk/
6. http://www.nih.org.pk.
7. www.environment.gov.pk/Biosftyrules-2005.pdf

7. Other Useful Links

1. http://apps.who.int/blueprint/mta-tool/
2. https://www.phe-culturecollections.org.uk/media/118559/managed-access-mta-for-monogenic-diabetes-sanger-hipsci-ipscs-eccw26002-17-.pdf
3. https://autm.net/surveys-and-tools/agreements/material-transfer-agreements/mta-toolkit/nih-mta-templates

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Approaches to Obtaining Informed Consent

Approach	How Consent is Obtained	Advantages	Disadvantages
Specific consent	Consent is taken for use of HBM for a specific research project. If participants give permission they are re-contacted for each new research project	Participant has full control, has full information about risk/benefit about the study	Cumbersome, not cost effective, may lead to loss of valuable data, difficult to locate participants and participants may have to be reached multiple times.
Open, generic Or blanket consent	Individual gives consent to any kind of future use of tissue and unlimited time duration for storage. Individual gives consent to any kind of future use of tissue and unlimited time duration for storage.	Extensive usage, least burdensome and most cost effective (no need to re-contact), no loss of data and participants avoid being recontacted.	Least control over use of HBM, loss of data of participants that may consent to some use, provides nothing about future risks or benefits so not truly informed consent and participants cannot reconsider about HBM use.
Tiered or broad consent	Individual may agree to various options for future use including general or specific consent on whether disease related or nonrelated, genetic use, time and use for commercialization. Participants is given a list of options that they can choose from. These include types of future research (genetic and commercial) and duration of storage.	Participant retains some control of HBM for future use, reduces burden on researchers as compared to specific consent and gives flexibility to participants and being recontacted.	Gives less leeway to participants if they want to participate in new research later which could not have been anticipated earlier and makes consent form to complex.
Presumed, opt out or implicit consent	Here it is presumed that the individual gives blanket consent for future use unless they opt-out. It is presumed that participants have given general consent unless they specifically opt out or do not give permission.	Lowest cost, no burden on researcher, maximizes usage of HBM participants avoid being re-contacted.	Least control over HBM use, all disadvantages of general consent and in addition requires specific action to prevent usage, it requires a high degree of awareness among general population

Sample Consent Form (WHO)

Certificate of Consent
A copy of CNIC/Form "B" of the Donor and researchers must be attached.

I wish my [TYPE OF SAMPLE i.e. blood, tissue, etc] I have provided for this research project to be sent outside Pakistan for/after this research.
(Tick one choice)

I do not allow my sample to be sent outside Pakistan.	
I allow my [*TYPE OF SAMPLE*] sample to be sent outside Pakistan [anywhere or except ----countries].	

I wish my [TYPE OF SAMPLE i.e. blood, tissue, etc] I have provided for this research project to be i destroyed after this research is over.
(Tick one choice)

I want my [*TYPE OF SAMPLE*] sample to be destroyed after ____ years.	
I give permission for my [TYPE OF SAMPLE] sample to be stored indefinitely	

I allow my [TYPE OF SAMPLE i.e. blood, tissue, etc] I have provided for this research project is unused or leftover after completion of this research to be store under following conditions. (Tick one choice from each of the following boxes).

I give permission for my [*TYPE OF SAMPLE*] sample to be stored and used in future research but only on the same subject as the current research project : [give name of current research]	
I give my permission for my [*TYPE OF SAMPLE*] sample to be stored and used in future research of **any type** which has been properly approved **except genetic research**.	
I give permission for my [*TYPE OF SAMPLE*] sample to be stored and used in future research except for research about [*NAME TYPE OF RESEARCH*].	
AND I give permission for my [*TYPE OF SAMPLE*] to be stored and used for commercial purposes.	

I want my identity to be removed from my [*TYPE OF SAMPLE*] sample.	
I want my identity to be kept with my [*TYPE OF SAMPLE*] sample.	

Questions about it and my questions have been answered to my satisfaction. I consent voluntarily to have my samples stored in the manner and for the purpose indicated above.
Print Name of Participant_____
Signature of Participant _____
Date (Day/month/year) _____

If illiterate
A literate witness must sign (if possible, this person should be selected by the participant and should have no connection to the research team). Participants who are illiterate should include their thumb-print as well.
I have witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.
Print name of witness_____
AND
Thumb print of participant
Signature of witness _____
Date (Day/month/year) _____

Statement by the researcher/person taking consent
I have accurately read out the information sheet to the potential participant, and to the best of my ability made sure that the participant understands that the following will be done:
1.
2.
3.
I confirm that the participant was given an opportunity to ask questions about the nature and manner of storage of the samples, and all the questions asked by the participant have been answered correctly and to the best of my ability. I confirm that the individual has not been coerced into giving consent, and the consent has been given freely and voluntarily.

A copy of this ICF has been provided to the participant.
Print Name of Researcher/person taking the consent_____
Signature of Researcher /person taking the consent_____

Date _____
Day/month/year

Annex III

Material transfer Agreement (MTA)

Preamble

(Name of Institute/ Organization/Ministry/Exporter/Donor/Owner) is/are committed to the implementation of Convention on biological Diversity (CBD) Nagoya Protocol as well as the relevant national and international --and requires its partners to act in a manner consistent with these multilateral agreements and Pakistan's access to genetic resources and benefits sharing laws and Export Control on goods, technologies, materials and equipment related to nuclear and biological weapons and their delivery system Act-2004 (SECA-2004).

Definitions

2. (Terms as those mentioned below and others that have been used in the draft MTA should be defined):-

2.1 Partners

2.2 Exporter/Donor/Owner

2.3 Recipient

2.4 Add other relevant Terms….

Provisions

3. This Material Transfer Agreement (MTA) is designed for sharing of _____material, originated in Pakistan (or------) and having the specifications contained in the schedule-I (Schedule-I shall cover specific details of the Nature and Type of Material to be transferred, number of samples to be Transferred, Quantity/Volume of material, Duration of Transfer/usage, purpose etc.) attached herewith, by -----Name of Institute/Lab, Address, country or etc.(give name of all the organizations involved) for – Purpose to the following terms and conditions

3.1 The recipient Institute reserves the right not to supply any animal, plant or fungal material or microorganism if such supply would be contrary to any terms attached, Material transfer Agreement or to the CBD, the Nagoya protocol, Pakistan's Access to genetic Resources and Benefit sharing laws or to the SECA-2004 or any other relevant Pakistani Laws.

3.2 The recipient will use the ---material, its progeny or derivatives only for the above mentioned specific purpose.

3.3 The Recipient shall not sell, transfer, provide access, re-export, distribute or use for profit or any other commercial application the Material, its progeny or derivative , without the explicit written consent of the ---(Name of institute)

3.4 The recipient If require capacity Building of any of the party to this MTA, appropriate and specific non monetary benefits may be identified and mentioned. For Guidance please refer to Pakistan Access to genetic Resources and Benefit Sharing Laws.

3.5 The recipient shall share fairly and equitably the benefits (appropriate and specific monetary/non-monetary benefits may be mentioned-Pakistan's draft Act on access to genetic resources and benefit sharing contains adequate guidance) arising from the use of material its progeny or derivatives in accordance with the CBD, the

Nagoya Protocol and access to genetic resources and benefit sharing laws of Pakistan.

3.6. The recipient shall acknowledge Pakistan as the country of origin of material in all written or electronic reports and publications resulting from the use of material originated from Pakistan, its progeny and derivatives and shall lodge a copy of all such publications and reports with the Permitting Authority and -----(Institute Name of Institute, Address)

3.7 The recipient shall take all appropriate and necessary measures to ensure safe and secure movement, import, export, handling of the material in accordance with the national/international conventions/agreements, laws and regulations and to contain the material, its progeny or derivatives so as to prevent the pilferage/theft/ exposure/unauthorized access/transfer of the material risking environment and or to susceptible species.

3.8 The Recipient shall maintain retrievable records (mention record keeping type e.g. printable /presentable and record keeping time period) linking the material to these terms of acquisition and to any accompanying data.

3.9 Unless otherwise indicated, copyright in all information or data ("Data") supplied with the material is owned by the Institute----Government of Pakistan.

3.10 The recipient makes no representation or warranty of any kind, either express or implied, as to the identity, safety, merchantability of fitness for any particular purpose of the material, its progeny or derivatives, or as to the accuracy of any Data supplied.

3.11 The Recipient will indemnify – Institute (Name and Address) Pakistan from any and all liability arising from the material its progeny or derivatives and/or the Data and from their use or transfer, including any ecological damage.

3.12 The recipient shall contact ---(Name of Institute) Pakistan to request prior permission or, where appropriate from the provider of the material to, for any activities not covered under the terms of this agreement.

3.13 This Material Transfer Agreement shall come into force upon the date of final signature and shall continue in effect (preferably for --- years which could be further extendable for --- years at each time, upon the consent of the Parties) until revoked by either party and or by both with mutual consent.

3.14 We (the person or body named) certify that we are the end user of the goods which are to be supplied by the exporter(named) will be used for peaceful purpose and will not be deviated from the stated end use. We further certify that neither the goods nor replicas and derivatives will be used for purpose connected with weapons of mass destruction and their means of delivery; that they will not be re-exported or otherwise re-sold or re-transferred if it is known or suspected that they are intended or likely to be used for malicious purposes; and that they will not be re-exported or otherwise re-sold or re-transferred without the explicit written consent of the Government of Pakistan.

3.15 We (the person or body named) certify that the samples, supplied by the exporter (named) will be sorted (duration) or disposed-off in the manner and for the purpose indicated in the agreement.

Signature/Agreement

4. I/We on behalf of (name of institute) agree to comply with the Terms and Conditions as stipulated above.

Accepted for (Exporter) (Name of Institute, Address)

Authorized Signature Date

Accepted for the Recipient (Name of Institute, Address)

Authorized Signature Date:

Annex-IV

Permission of National Institute of Health (NIH) regarding Export/transfer of Pathogen, infected/suspected samples or derivatives

Permission form National Institute of Health NIH

Name of Project/ research	Description of Nature of HBM Technical Specification (Name pathogen)	Number/ Quantity	Shipment type/ category/ Packaging/mode of transport	Purpose of Export	Destination of export/ Country	Remarks

Undertaking:

I ----------hereby agree that the information provided above is true. I have completed all the legal and codal formalities/requirements of SECDIV and NBC and all the related documents are attached herewith.

Name of Researcher _____

Signature of Researcher _____

Date _____

Comments of the (ICC) Committee/Management on Export of HBM, NIH

Remarks of PCO (Principle Compliance Officer)/PSO PHLD NIH

Date: Signature **(Name, Designation, Stamp)**

Decision by the CEO/Chief PHLD NIH Date:

Signature **(Name, Designation, Stamp)**